Clinical Update

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Top 25 Drugs in the United States, 2000
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As the general population ages and advances in medical technologies and pharmacotherapeutics continue to emerge, increasingly complex medication profiles are evident in our patients. The purpose of this Clinical Update is to summarize the mechanism of action, indications, adverse effects, and interactions of concern to the dentist for the top 25 drugs prescribed in the United States during the year 2000.

CARDIOVASCULAR DRUGS

Norvasc (*amlodipine*) is a calcium (Ca^{++}) channel blocker used to treat hypertension (HTN) and stable angina (1). It impedes the entry of Ca^{++} into the slow Ca^{++} channels of the vascular smooth muscle and cardiac muscle, which produces dilation of both the coronary and peripheral blood vessels and a corresponding decrease in peripheral resistance and blood pressure (BP).

Adverse Effects: Edema, headache (HA), flushing, nausea, dizziness, orthostatic hypotension, dry mouth, altered taste, gingival enlargement.

Drug Interactions: There are no significant drug interactions.

Lasix *(furosemide),* Maxzide/Dyazide *(triamterene/HCTZ),* and ***hydrochlorthiazide*** are diuretics used to treat HTN and edema associated with congestive heart failure, chronic renal and liver disease. They cause a net loss of Na^+ and water by increasing the urinary excretion of salt and water and by reducing reabsorption of renal Na^+.

Adverse Effects: Dizziness, HA, xerostomia, erythema multiforme, electrolyte imbalance (potassium loss with furosemide), and orthostatic hypotension are frequently reported.

Drug Interactions: Corticosteroids enhance hypokalemia which may increase the risk for cardiac arrhythmias.

Tenormin *(atenolol)* is a cardioselective beta-blocker used to manage HTN and angina pectoris. It blocks B-1 receptors in the heart and kidney which decreases heart rate, oxygen consumption, BP, and the secretion of renin by the kidney.

Adverse effects: Dry mouth, hypotension, fatigue, dizziness, bradycardia, and dyspnea (only at high doses).

Drug interactions: Prolonged use (> 3 weeks) of nonsteroidal antiinflammatory drugs (NSAIDs) may decrease the hypotensive effects. Epinephrine may increase BP.

Dental considerations: Vital signs should be monitored at each appointment. To avoid orthostatic hypotension, the patient should be raised slowly from the supine position and sit for 2 minutes prior to dismissal. Minimize stress, exercise caution with vasoconstrictors, and monitor salivary flow.

ANTILIPID DRUGS

Lipitor (*atorvastatin*) is a HMG-CoA reductase inhibitor used to lower total and LDL ("bad") cholesterol by inhibiting the rate-limiting step in cholesterol synthesis (2). It does not effect HDL ("good") cholesterol levels.

Adverse Effects: HA, anemia, dysgeusia, neuropathy, erythema multiforme, and myopathy.

Drug Interactions: The risk of myopathy is increased with the concurrent administration of cyclosporine, erythromycin, clarithromycin, fluconazole and ketoconazole.

ANTIHISTAMINES

Claritin (*loratadine*) is a non-sedating histamine-1 (H_1) receptor antagonist that acts by competing reversibly for H_1 receptor sites. It relieves symptoms of seasonal allergic rhinitis of recent onset, with less drowsiness than other antihistamines and may also benefit patients with urticaria (hives) and angioedema.

Adverse Effects: Dry mouth, dizziness.

Drug Interactions: Erythromycin and ketoconazole may increase levels of *Claritin*, but no increase in adverse effects are noted.

Dental Considerations: Assess salivary flow.

ANTISECRETORY DRUGS

Prilosec (*omeprazole*) suppresses gastric acid secretion by inhibiting the proton pump enzyme system of parietal cells in the stomach (3). It is used in short-term treatment (up to 4 weeks) for healing and symptomatic relief of active duodenal and peptic ulcers, erosive esophagitis and hypersecretory conditions.

Adverse Effects: HA, diarrhea, dry mouth, altered taste, mucosal atrophy of the tongue, rash.

Drug Interactions: The metabolism of diazepam and warfarin may be decreased. Prilosec decreases the absorption of ketoconazole, itraconazole, and vitamin B_{12}.

Dental Considerations: Aspirin or NSAIDs should be avoided.

ANTIDEPRESSANTS

Prozac (*fluoxetine*), Zoloft (*sertraline*), Paxil (*paroxetine*) are "selective serotonin reuptake inhibitors" used to treat depression. They selectively inhibit serotonin reuptake, increasing concentration of the neurotransmitter in the CNS (4). This is associated with an improvement of mood, appetite, and sleep.

Adverse Effects: Nausea, dizziness, HA, nervousness, insomnia, dysgeusia, xerostomia, drowsiness, and postural hypotension.

Drug Interactions: Alcohol or other CNS depressants may increase CNS depression. Aspirin and other highly protein bound drugs may increase the side effects of Prozac.

Dental Considerations: Assess salivary flow.

ORAL HYPOGLYCEMICS

Glucophage *(metformin)* is an oral hypoglycemic agent used in mono or combination therapy for Type 2 diabetes mellitus. It does not increase insulin secretion but works by decreasing glucose production in the liver and by increasing glucose cellular uptake and utilization by target cells (5). It does not cause hypoglycemia.

Adverse Effects: Unpleasant GI effects such as nausea, vomiting, diarrhea and a *metallic taste* have been reported. Lactic acidosis is a very rare occurrence. Metformin can decrease absorption of vitamin B_{12} and folic acid resulting in a deficiency of these vitamins.

Drug Interactions: Oral corticosteroids may elevate blood glucose levels.

Dental Considerations: Assess the patient's level of glucose con-

trol prior to treatment.

ANALGESICS

Vicodin ***(Hydrocodone with acetaminophen),*** **Darvocet-N** ***(propoxyphene napsylate with acetaminophen), acetaminophen w/ codeine,*** **Motrin** ***(ibuprofen),*** **Celebrex (*celecoxib*)**

The first three drugs are combination opioid analgesics that bind to opiate receptors in the brain to inhibit ascending pain pathways and decrease pain perception. **Propoxyphene** is a weak opioid analgesic. Acetaminophen inhibits the synthesis of prostaglandins in the CNS and peripherally blocks pain impulses. These 3 agents are used to treat mild to moderate dental pain. **Ibuprofen** is a non-selective NSAID that inhibits prostaglandin synthesis by blocking cyclooxygenase activity and is used to manage dental pain and swelling. **Celebrex** is a selective cyclooxygenase-2 inhibitor used to treat osteoarthritis and rheumatoid arthritis. Normal doses of **Celebrex** do not affect platelet aggregation or bleeding time.

Adverse Effects: For combination opioids: dry mouth, dizziness, respiratory depression/dyspnea, nausea, vomiting, constipation, sedation. For ibuprofen: gastrointestinal irritation, ulceration and bleeding, decreased platelet aggregation and function (6). Initial studies showed Celebrex to cause less gastrointestinal toxicity than nonselective NSAIDS, but more recent reports suggest otherwise (6,7). Celebrex may be associated with an increased risk for thrombotic cardiovascular events (8).

Drug Interactions: Opioids potentiate all CNS depressants. NSAIDs can decrease the effectiveness of hypertension medications while fluconazole may increase levels of Celebrex. Concurrent use of Celebrex and warfarin may increase the International Normalized Ratio (INR) and risk for bleeding.

Dental Considerations: Avoid prescribing NSAIDS in the 3rd trimester of pregnancy. There is abuse potential with chronic use of opioids (6,7).

HORMONE REPLACEMENTS

Premarin (*conjugated estrogen*), Synthroid ***(levothyroxine)***

Premarin is prescribed to relieve postmenopausal symptoms and prevent osteoporosis. It appears to decrease the risk for major coronary events in women without previous heart disease and is commonly prescribed with **Provera** ***(medroxyprogesterone***) to prevent cervical/endometrial cancer. **Synthroid** is used as replacement or supplemental therapy in hypothyroidism.

Adverse Effects: Excess Synthroid increases the metabolic rate and may result in tachycardia, tremors, nervousness, insomnia, diarrhea, weight loss, heat intolerance, and fever.

Drug Interactions: Premarin taken with hydrocortisone may cause corticosteroid-induced toxicity. Synthroid may enhance the effect of Coumadin *(*increase bleeding) and decrease the effectiveness of oral hypoglycemics.

Dental Considerations: Hypothyroid patients may be more sensitive to CNS depressants, while hyperthyroid patients are very sensitive to vasoconstrictors.

BRONCHODILATORS

Albuterol sulfate **(Proventil, Ventolin)** relaxes bronchial smooth muscle (by its action on beta-2 adrenergic receptors) and relieves acute asthma-induced bronchospasm.

Adverse Effects: Fine finger tremors and tachycardia.

Dental Considerations: Patients should have their albuterol inhaler readily available at the dental appointment. Rarely, asthmatics can be sensitive to sulfites (preservative in local anesthetic); also NSAIDs may precipitate an asthmatic attack (6).

ANTIANXIETY DRUGS

Xanax ***(Alprazolam)*** is a benzodiazepine that binds to GABA (gamma-aminobutyric acid) receptors in the CNS to facilitate GABA and block arousal nerve impulses. It is used to allay anxiety and treat panic disorders.

Adverse Effects: Drowsiness, dizziness, orthostatic hypotension, blurred vision, HA, and abuse potential.

Drug Interactions: Additive CNS depression may occur with concomitant use of other CNS depressants.

Dental Considerations: Dry mouth can be significant (6,9).

ANTIMICROBIAL DRUGS

Keflex ***(cephalexin), amoxicillin,*** **Trimox (*amoxicillin*), Zithromax (*azithromycin*)**

Cephalexin is a broad-spectrum cephalosporin that inhibits bacterial cell wall synthesis and has a spectrum of activity slightly wider than penicillin. It is used to premedicate patients at risk for prosthetic joint infection, as an alternative antibiotic in the treatment of orofacial infections and prevention of subacute bacterial endocarditis (SBE) in penicillin-allergic patients. **Amoxicillin** is an extended spectrum beta-lactam antibiotic that inhibits bacterial cell wall synthesis and is the standard SBE prophylactic regimen for dental patients who are at risk. **Zithromax** is a macrolide antibiotic that inhibits bacterial RNA-dependent protein synthesis and has a spectrum of activity similar to erythromycin. It is an alternative antibiotic for the treatment of orofacial infections and prevention of SBE.

Adverse Effects: Allergy, diarrhea, nausea, vomiting, abdominal pain (all); rash, seizure, superinfection (amoxicillin).

Drug Interactions: Although controversial, the efficacy of oral contraceptives may be reduced by amoxicillin. It may also increase the effects of warfarin.

Dental Considerations: Prolonged use of penicillins can lead to oral candidiasis. Cephalexin is contraindicated in patients with an immediate-type allergic reaction to penicillin (6).

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Top 25 Prescriptions in the United States, 2000
Adapted from RxList.com

2000 Rank	Product	Generic	Drug Class
1	**Hydrocodone w/ APAP**	hydrocodone w/ acetaminophen	combination narcotic analgesic
2	**Lipitor**	atorvastatin	cholesterol-lowering agent
3	**Premarin Tabs**	conjugated estrogen	estrogen hormone supplement
4	**Synthroid**	synthetic L-thyroxine	thyroid hormone
5	**Atenolol**	(generic)	selective *B*-blocker
6	**Furosemide**	(generic)	loop diuretic (non K^+ sparing)
7	**Prilosec**	omeprazole	antisecretory compound (GI acid)
8	**Albuterol (inhaler)**	albuterol sulfate (generic)	$beta_2$-agonist bronchodilator
9	**Norvasc**	amlodipine besylate	2^{nd} gen. calcium channel blocker
10	**Alprazolam**	(generic)	benzodiazepine anxiolytic
11	**Propoxyphene NAP w/ APAP**	propoxyphene napsylate w/ acetaminophen	combination synthetic narcotic analgesic
12	**Glucophage**	metformin HCl	biguanide-type oral hypoglycemic
13	**Cephalexin**	cephalexin (generic)	cephalosporin (1st generation)
14	**Amoxicillin**	amoxicillin (generic)	extended spectrum beta lactam
15	**Claritin**	loratidine	H_1-receptor antagonist non-sedating antihistamine)
16	**Trimox**	amoxicillin	extended spectrum beta-lactam
17	**Hydrochlorthiazide**	(generic)	diuretic
18	**Zoloft**	sertraline	antidepressant (SSRI class)
19	**Zithromax**	azithromycin	2^{nd} gen. macrolide antibiotic
20	**Prozac**	fluoxetine	antidepressant (SSRI class)
21	**Ibuprofen**	(generic)	NSAID
22	**Paxil**	paroxetine	antidepressant (SSRI class)
23	**Triamterene/HCTZ**	(generic)	combination diuretic
24	**Celebrex**	celecoxib	NSAID (COX-2 inhibitor**)**
25	**Acetaminophen w/codeine**	(generic)	combination narcotic analgesic